

CURRICULUM VITAE

ROBERT M. HOFFMAN

January 2000

Exhibit 1 RMH

*CURRICULUM VITAE***ROBERT M. HOFFMAN****RECEIVED**
MAY 21 2002
TECH CENTER 1600/2900**OFFICES:**

AntiCancer, Inc.
7917 Ostrow Street
San Diego, California 92111
TEL: (619) 654-2555
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Department of Surgery
University of California, San Diego
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200 West Arbor Drive
San Diego, California 92103-8402
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BIRTH DATE:

June 19, 1944
Greenwich, Connecticut

EDUCATION:

Ph.D. (Biology)
Harvard University
Cambridge, Massachusetts

1971

B.A. (Biology)
State University of New York
Buffalo, New York

1965

**PRESENT
POSITIONS:**

President, Chairman of Board and CEO
AntiCancer, Inc.
San Diego, California

1984-present

Professor
Department of Surgery
University of California, San Diego
Medical Center
200 West Arbor Drive
San Diego, California 92103-8220

1995-present

MAJOR RESEARCH ACCOMPLISHMENTS:

1. Development of highly-selective anti-methionine cancer therapy based on methioninase.
2. The first DNA-containing liposomes - the enabling technology for *in vivo* gene therapy.
3. Development of a "patient-like" animal model for cancer - "MetaMouseTM".
4. Development of an *in vivo*-like model of human tumor culture and drug-sensitivity testing.
5. Development of an *in vitro* hair growth model from human and animal skin.
6. Development of a hair follicle-specific drug and gene targeting system.
7. Discovery of the governing step of metastasis.
8. The use of green fluorescent protein to study cancer metastasis and for cancer gene therapy.

POSTDOCTORAL TRAINING:

Department of Biology
Harvard University
With the late Professor John R. Raper. 1971-1973

Massachusetts General Hospital 1973-1975

Harvard Medical School
With Dr. Richard W. Erbe and Professor John W. Littlefield 1976-1977

The Shemyakin Institute of Bioorganic Chemistry
Academy of Sciences, Moscow, USSR
With Professor L.D. Bergelson 1976-1977

Weizmann Institute of Science
Rehovot, Israel
With Dr. Carol Prives 1978

PREVIOUS ACADEMIC POSITIONS:

Instructor of Pediatrics
Harvard Medical School
Massachusetts General Hospital 1975-1979

Assistant Professor, Department of Pediatrics
University of California, San Diego, School of Medicine
School of Medicine 1979-1983

Associate Professor, Department of Pediatrics
University of California, San Diego
School of Medicine 1983-1990

Professor, Department of Pediatrics
University of California, San Diego
School of Medicine

1990-1995

PROFESSIONAL SOCIETIES:

1. Society for *In Vitro* Biology
2. American Association of Cancer Research
3. American Society for Clinical Oncology
4. Society of Surgical Oncology
5. American Society for Cell Biology
6. Metastasis Research Society
7. Japanese Cancer Association
8. Japanese Metastasis Research Society
9. Japanese Society of Human Cell
10. Preclinical Therapeutic Model Group of the
European Organization for Research and Treatment of Cancer

BOARDS:

Ad-Hoc Reviewer
National Cancer Institute

1986-present

EDITORIAL BOARDS:

Anticancer Research
In Vitro Cellular and Developmental Biology

1985-present

1987-present

TEACHING AT THE UNIVERSITY OF CALIFORNIA, SAN DIEGO:

Biology 112: "Cell and Molecular Biology"
Spring and Fall
With Professor Gordon Sato

1980

Pediatrics 233: "Genes and Cancer"
Winter

1982-1994

Pediatrics 235: "New Biological Approaches to Cancer Prevention and Treatment"
Spring

1983-1994

Pediatrics 237: "Biochemical Genetics of Aging"
Fall

1984-1994

UNIVERSITY COMMITTEES:

Admissions Committee
University of California, San Diego
School of Medicine

1983-1985

Electives Committee
University of California, San Diego
School of Medicine

1989-1990

HONORS AND AWARDS:

Honorary Professor
Harbin Medical University
Harbin, China

1994

Honorary Member
Keio University Department of Surgery
Tokyo, Japan

1991

A.N. Belozersky Medal
Moscow State University

1990

Research Career Development Award
National Cancer Institute

1982-1987

Fellow of the Leukemia Society of America

1979-1981

Fellow of the Medical Foundation of Boston

1976-1977

United States National Academy of Sciences
Exchange Fellowship
Shemyakin Institute of Bioorganic Chemistry
Moscow, USSR.

1976-1977

Postdoctoral Fellowship Awardee
National Institutes of Health

1974,76,78

National Institutes of Health
Postdoctoral Training Grant Fellow
Harvard Medical School

1973-1974

Postdoctoral Research Fellow
Harvard University

1971-1973

National Institutes of Health
Training Grant Predoctoral Fellowship
Harvard University

1966-1971

Phi Beta Kappa
State University of New York
Buffalo, New York

1964

PLENARY LECTURES:

International Symposium on "The biochemistry
of S-adenosylmethionine as a basis of drug design"

Bergen Norway

Lecture entitled "Cancer, methionine and transmethylation."

1985

Federation of American Societies for
Experimental Biology Summer Research Conference
entitled "Folic acid, B-12, and one-carbon metabolism"

Saxtons River, Vermont

Lecture entitled "Altered methionine metabolism and
transmethylation in human cancer cells."

1986

Gordon Research Conference on Cancer

New London, New Hampshire

Lecture entitled "Methionine, transmethylation and cancer."

1987

Invited lecturer, Tissue Culture Association Conference

Las Vegas, Nevada

Lecture entitled "Partitioning of methyl groups in cancer and normal cell types."

1988

Federation of American Societies for
Experimental Biology Summer Research Conference

Copper Mountain, Colorado

Lecture entitled "Cancer, methionine metabolism and transmethylation."

1989

Invited Lecturer, Dae Han Biochemical Society

Seoul, Korea

Lecture entitled "Altered methionine metabolism, unbalanced
global cellular transmethylation and cancer."

1990

Invited Lecturer, Korean Association of Molecular Biology

Pusan, Korea

Lecture entitled "Rational evaluation and design of cancer drugs."

1990

Third International Conference of Anticancer Research

Marathon, Greece

Lecture entitled "The development of clinically relevant in vitro and in vivo
preclinical models: Three-dimensional gel-supported in vitro histoculture and
orthotopic implantation and metastasis of human tumors in nude mice."

1990

- Invited Lecturer, Regina Elena Cancer Center
Rome, Italy
Lecture entitled "Patient-like in vitro and in vivo pre-clinical models of human cancer." 1991
- Gordon Research Conference on Cancer Chemotherapy
New London, New Hampshire
Lecture entitled "Orthotopic-transplantation animal models for the identification of new anticancer drugs." 1992
- Fourth International Congress of the Metastasis Research Society
Paris, France
Lecture entitled "The nude mouse comes to the cancer clinic: Metastatic models of the major cancer types constructed by orthotopic transplantation of histologically-intact patient specimens." 1992
- First Congress of the International Society for Experimental Microsurgery 1992
Rome, Italy
Lecture entitled "Microsurgery, orthotopic human tumor transplantation and the nude mouse: Patient-like metastatic models of human cancer."
- Keystone Symposium on Discovery and Development of Therapeutic Compounds 1993
Snowmass, Colorado
Session Chairman., Lecture entitled "Orthotopic models for treatment evaluation in vivo using histologically-intact cancer patient specimens."
- FASEB Summer Conference. 1993
Copper Mountain, Colorado
Lecture entitled "MetaMouse: the nude mouse comes to the cancer clinic via orthotopic transplantation of architecturally-intact patient tumors."
- Hellenic Society For Breast Cancer Research, First Int'l Congress 1993
Corfu, Greece
Lecture entitled "Patient-like cancer models and therapeutics specific for cancer- an approach to the next generation of treatment"
- FASEB Summer Conference 1994
Copper Mountain, Colorado
Lecture entitled "Tissue architecture and metastases"
- Japan Society of Human Cell Meeting 1995
Toyoma City, Japan
Lecture entitled "In vitro drug response assays are clinically useful in cancer"

- Hellenic Society For Breast Cancer Research, Second Int'l Congress
Kos Island, Greece
Lecture entitled "Methioninase (AC9301): A selective antitumor agent
with a new mechanism of action." 1995
- 6th International Congress on Anticancer Treatments
Paris, France
Lecture entitled "Pilot phase I clinical trial of methioninase: serum
depletion of methionine without acute toxicity." 1996
- 6th International Congress on Anticancer Treatments
Paris, France
Lecture entitled "The gelatinase-A Inhibitor CT1746 arrests human colon
tumor growth and spread and increases survival in a patient like orthotopic
model in nude mice." 1996
- IBC USA Alopecia Conference
San Diego, California
Lecture entitled "The feasibility of targeted selective gene therapy of the
hair follicle." 1996
- Shanghai International Symposium on Liver Cancer & Hepatitis
Shanghai, China
Lecture entitled "Liver colonization capability governs metastatic potential" 1996
- Cambridge Healthtech Institute's Engineered Animal Models
Baltimore, Maryland
Lecture entitled "MetaMouse™ Models of Cancer: Clinically Relevant
Orthotopic Models of Cancer Growth and Metastasis" 1996
- Third International Conference of the Asian Clinical Oncology Society (ACOS)
Kunming, China
Lecture entitled "Taking chemotherapy from random to rational with the
histoculture drug response assay" 1996
- The International Congress on Human Cell and Cell Culture
Tokyo, Japan
Lecture entitled "Nutritional regulation of cancer growth by use of
methioninase: possible apoptotic cell kill mechanism" 1996
- The Sixth International Congress of the Metastasis Research Society
Gent, Belgium
Lecture entitled "Surgical Orthotopic Implantation (SOI): A new approach
to develop clinically-relevant models of human metastatic cancer in
immunodeficient rodents" 1996

- IBC's Alopecia Conference 1996
Washington, D.C.
Lecture entitled "Hair Follicle Targeting of Large and Small Molecules with Topical Liposomes"
- First Panhellenic Congress of Tumors Markers with International Participation 1996
Athens, Greece
Lecture entitled "Methionine dependence as a Possible Universal Therapeutic Tumor Marker"
- Seventh International Congress on Anticancer Treatment (SOMPS) 1997
Paris, France
Lecture entitled "R-Methioninase as a potential universal apoptotic antitumor agent"
- Seventh International Congress on Anticancer Treatment (SOMPS) 1997
Paris, France
Lecture entitled "Acquisition of broad range multidrug resistance in recurrent breast cancer"
- IBC's Drug Discovery Approaches to Cosmeceuticals Conference 1997
East Rutherford, NJ
Lecture entitled "Hair producing histoculture skin for the discovery of a new generation of hair follicle targeted cosmeceuticals and therapeutics"
- 30th Annual Meeting of the Japanese Research Society for Appropriate Cancer Chemotherapy 1997
Tokyo, Japan
Lecture entitled "Histoculture Drug Response Assay"
- IBC's Delivery Technologies for Cosmetic Ingredients Conference 1997
Philadelphia, PA
Lecture entitled "Cosmetic and therapeutic molecules targeted to hair follicles by topical liposomal application"
- 6th Hellenic Congress on Senology and the 3rd International Congress of the Hellenic Society for Breast Cancer Research 1997
Alexandroupolis, Greece
Lecture entitled "Cachexia in breast cancer and elevated amino-acid requirements of tumors: Selective biological targets for therapy"

- FASEB Summer Research Conference on Biological Methylation 1997
Saxtons River, Vermont
Lecture entitled "Alterations in methionine dependence and transmethylation
in cancer: methioninase for therapy"
- 3rd International Symposium on Polymer Therapeutics 1998
London, England
Lecture entitled "Polyethylene glycol conjugation of recombinant methioninase
for cancer therapy"
- 8th International Congress on Anti-Cancer Treatment 1998
Paris, France
Lecture entitled "Polyethylene glycol conjugation of recombinant methioninase
for cancer therapy"
- Gordon Research Conference on Lasers in Medicine and Biology 1998
Meriden, NH
Lecture entitled "Green fluorescent protein: A new light to study metastasis and
angiogenesis"
- 25th Balken Medical Week Conference 1998
Ioannina, Greece
Lecture entitled "Methioninase. A new selective cancer therapy"
- 7th Annual Meeting of the Japanese Association for Metastasis Research 1998
Sapporo, Japan
Lecture entitled "Green fluorescent protein: A new light to study the role of
angiogenesis in metastasis"
- SPIE's International Symposium on Biomedical Optics 1999
San Jose, CA
Lecture entitled "Green fluorescent protein: A new light to visualize metastasis
and angiogenesis in cancer"
- 2nd International Symposium on GFP – The Green Fluorescent Protein 1999
San Diego, CA
Lecture entitled "Fluorescent optical tumor imaging (FOTI) of human cancers
in live nude mice"
- Fourth International Conference of the Asian Clinical Oncology Society (ACOS) 1999
Bali, Indonesia
Lecture entitled "Individualizing cancer chemotherapy by tumor histoculture"

Publications of Robert M. Hoffman, Ph.D.

1. Hoffman, R.M., and Raper, J.R. Genetic restriction of energy conservation in *Schizopyllum*. Science 171, 418-419, 1971.
2. Hoffman, R.M. and Raper, J.R. Lowered respiratory response to adenosine diphosphate of mitochondria isolated from a mutant-B strain of *Schizopyllum commune*. J. Bacteriol. 110, 789-791, 1972.
3. Raper, J.R. and Hoffman, R.M. *Schizopyllum commune*. In: Handbook of Genetics. 3, R King (ed.), New York, Plenum Press, 597-626, 1974.
4. Hoffman, R.M. and Raper, J.R. Genetic impairment of energy conservation in development of *schizopyllum*: Efficient mitochondria in energy-starved cells. J. Gen. Microbiol. 82, 67-75, 1974.
5. Hoffman, R.M. and Erbe, R.W. High *in vivo* rates of methionine biosynthesis in transformed human and malignant rat cells auxotrophic for methionine. Proc. Natl. Acad. Sci. USA 73, 1523-1527, 1976.
6. Williams, J., Hoffman, R.M. and Penman, S. The extensive homology between mRNA sequences of normal and SV40-transformed human fibroblasts. Cell 11, 901-907, 1977.
7. Hoffman, R.M., Jacobsen, S. J. and Erbe, R.W. Reversion to methionine independence by malignant rat and SV40-transformed human fibroblasts. Biochem. Biophys. Res. Commun. 82, 228-234, 1978.
8. Hoffman, R.M., Margolis, L.B. and Bergelson, L.D. Binding and entrapment of high molecular weight DNA by lecithin liposomes. FEBS Letters 93, 365-368, 1978.
9. Hoffman, R.M., Jacobsen, S.J. and Erbe, R.W. Reversion to methionine independence in SV40-transformed human and malignant rat fibroblasts is associated with altered ploidy and altered properties of transformation. Proc. Natl. Acad. Sci., USA 76, 1313-1317, 1979.
10. Jacobsen, S.J., Hoffman, R.M. and Erbe, R.W. Regulation of methionine adenosyltransferase in normal diploid and SV40-transformed human fibroblasts. J. Natl. Cancer Inst. 65, 1237-1244, 1980.
11. Hoffman, R.M. and Jacobsen, S.J. Reversible growth arrest in SV40-transformed human fibroblasts. Proc. Natl. Acad. Sci., USA 77, 7306-7310, 1980.
12. Rubnitz, J.E., Jacobsen, S.J. and Hoffman R.M. Constitutive behavior of methionyl-tRNA synthetase compared to repressible behavior of methionine adenosyltransferase in mammalian cells. Biochem. Biophys. Acta Reviews on Cancer 577, 269-273, 1981.

13. Dials, E.S., Plent, M.M., Coalson, D.W. and Hoffman, R.M. DNA methylation in normal and SV40-transformed human fibroblasts. *Biochem Biophys. Res. Commun.* 102, 1379-1384, 1981.
14. Hoffman, R.M., Coalson, D. W., Jacobsen, S.J. and Erbe, R.W. Folate polyglutamate and monoglutamate accumulation in normal and SV40-transformed human fibroblasts. *J. Cell. Physiol.* 109, 497-505, 1981.
15. Hoffman, R.M. Methionine dependence in cancer cells - a review. *In Vitro* 18, 421-428, 1982.
16. Coalson, D.W., Mecham, J.O., Stern, P.H., and Hoffman, R.M. Reduced availability of endogenously synthesized methionine for S-adenosylmethionine formation in methionine-dependent cancer cells. *Proc. Nat. Acad. Sci., USA* 79, 4248-4251, 1982.
17. Dials, E.S. and Hoffman, R.M. DNA methylation levels in normal and chemically-transformed mouse 3T3 cells. *Biochem. Biophys. Res. Commun.* 104, 1489-1494, 1982.
18. Dials, E.S. and Hoffman, R.M. Hypomethylation of HeLa cell DNA and the absence of 5-methylcytosine in SV40 and adenovirus (type 2) DNA: analysis by HPLC. *Biochem. Biophys. Res. Commun.* 107, 19-26, 1982.
19. Stern, P.H., Mecham, J. O. and Hoffman, R.M. Preparation of [³⁵S]homocysteine thiolactone free of [³⁵S]methionine. *J. Biochemical and Biophysical Methods* 7, 83-88, 1982.
20. Dials, E.S. and Hoffman, R.M. Epstein-Barr HR-1 virion DNA is very highly methylated. *J. Virology* 45, 482-483, 1983.
21. Stern, P.H., Mecham, J.O., Wallace, C.D. and Hoffman, R.M. Reduced free-methionine in methionine-dependent SV40-transformed human fibroblasts synthesizing apparently normal amounts of methionine. *J. Cell. Physiol.* 117, 9-14, 1983.
22. Dials, E.S., Cheah, M.S.C., Rowitch, D. and Hoffman, R.M. The extent of DNA methylation in human tumor cells. *J. Natl. Cancer Inst.* 71, 755-764, 1983.
23. Oden, K.L., Carson, K., Mecham, J.O., Hoffman, R.M. and Clarke, S. S-adenosylmethionine synthetase in cultured normal and oncogenically-transformed human and rat cells. *Biochem. Biophys. Acta* 870, 270-277, 1983.
24. Mecham, J.O., Rowitch, D., Wallace, C.D., Stern, P.H. and Hoffman, R.M. The metabolic defect of methionine dependence occurs frequently in human tumor cell lines. *Biochem. Biophys. Res. Commun.* 117, 429-434, 1983.
25. Stern, P.H., Wallace, C.D. and Hoffman, R.M. Altered methionine metabolism occurs in all members of a set of diverse human tumor cell lines. *J. Cell. Physiol.* 119, 29-34, 1984.

26. Hoffman, R.M. Altered methionine metabolism, DNA methylation and oncogene expression in carcinogenesis: a review and synthesis. *Biochem. et Biophys. Acta Reviews on Cancer* 738, 49-87, 1984.
27. Cheah, M.S.C., Wallace, C.D. and Hoffman, R.M. Hypomethylation of DNA in human cancer cells: a site-specific change in the c-myc oncogene. *J. Natl. Cancer Inst.* 73, 1057-1065, 1984.
28. Stern P.H. and Hoffman, R.M. Elevated overall rates of transmethylation in cell lines from diverse human tumors. *In Vitro - Rapid Commun. in Cell Biology* 20, 663-670, 1984.
29. Hoffman, R.M. Altered methionine metabolism and transmethylation in cancer. *Anticancer Res.* 5, 1-30, 1985.
30. Hoffman, R.M. and Stern, P.H. Cancer, methionine and transmethylation. In *Biological Methylation and Drug Design*, Borchardt, R.T., Creveling C.R. and Ueland, P.M, eds., Clifton, New Jersey, The Humana Press Inc., pp. 215-225, 1986.
31. Stern, P.H. and Hoffman, R.M. Enhanced in vitro selective toxicity of chemotherapeutic agents for human cancer cells based on a metabolic defect. *J. Natl. Cancer Inst.* 76, 629-639, 1986.
32. Freeman, A.E. and Hoffman, R.M. In vivo-like growth of human tumors in vitro. *Proc. Natl. Acad. Sci., USA* 83, 2694-2698, 1986.
33. Stern, P.H. and Hoffman, R.M. The chemical synthesis of high specific-activity [³⁵S]adenosylhomocysteine. *Analytical Biochem.* 158, 408-412, 1986.
34. Vescio, R.A., Redfern, C.H., Nelson, T.J., Ugoretz, S. Stern, P.H. and Hoffman, R.M. *In vivo*-like drug responses of human tumors growing in three-dimensional, gel-supported, primary culture. *Proc. Natl. Acad. Sci., USA* 84, 5029-5033, 1987.
35. Hoffman, R.M. Altered methionine metabolism and unbalanced methylation: a possible basis for the dynamic phenotype of cancer. *Absorption and Utilization of Amino Acids*, (1989) CRC Press, Boca Raton, Florida M. Friedman (ed.) pp. 1-7.
36. Hoffman, R.M., Monosov, A.Z., Connors, K.M., Herrera, X. and Price, J.H. A general native-state method for determination of proliferation capacity of human normal and tumor tissues *in vitro*. *Proc. Natl. Acad. Sci., USA* 86, 2013-2017, 1989.
37. Wallen, J.W., Cate, R.L., Kiefer, D.M., Riemen, M.W., Martinez, D., Hoffman, R.M., Donahoe, P.K., Von Hoff, D.D., Pepinsky, B. and Oliff, A. Minimal antiproliferative effect of recombinant Mullerian Inhibiting Substance on gynecological tumor cell lines and tumor explants. *Cancer Res.* 49, 2005-2011, 1989.

38. Vescio, R.A., Connors, K.M., Youngkin, T., Bordin, G.M, Robb, J.A, Umbreit, J.N. and Hoffman, R.M. Cancer biology for individualized cancer therapy: Correlation of growth fraction index in native-state histoculture with tumor grade and stage. *Proc. Natl. Acad. Sci., USA* 87, 691-695, 1990.
39. Hoffman, R.M. Unbalanced transmethylation and the perturbation of the differentiated state leading to cancer. *BioEssays* 12, 163-166, 1990.
40. Vescio, R.A., Connors, K.M., Bordin, G.M., Robb, J.A., Youngkin, T, Umbreit, J.N. and Hoffman, R.M. The distinction of small cell and non-small cell cancer by growth in native-state histoculture. *Cancer Res.* 50, 6095-6099, 1990.
41. Wilson, W.W. and Hoffman, R.M. Methylation of intact chromosomes by bacterial methylases in agarose plugs suitable for pulsed-field electrophoresis. *Analytical Biochem.* 191, 370-375, 1990.
42. Hoffman, R.M. *In vitro* sensitivity assays in cancer: A review, analysis and prognosis. *J. Clin. Lab. Anal.* 5, 133-143, 1991.
43. Li, L., Margolis, L.B. and Hoffman, R.M. Skin toxicity determined *in vitro* by three-dimensional, native-state histoculture. *Proc. Natl. Acad. Sci.* 88, 1908-1912, 1991.
44. Robbins, K.T., Varki, N.M., Storniolo, A.M., Hoffman, H. and Hoffman, R.M. Drug response of head and neck tumors in native-state histoculture. *Archives of Otolaryngol. Head and Neck Surg.* 117, 83-86, 1991.
45. Hoffman, R.M. Three-dimensional histoculture: Origins and applications in cancer research. *Cancer Cells* 3, 86-92, 1991.
46. Vescio, R.A., Connors, K.M., Kubota, T. and Hoffman, R.M. Correlation of histology and drug response of human tumors grown in native-state three-dimensional histoculture and in nude mice. *Proc. Natl. Acad. Sci., USA* 88, 5163-5166, 1991.
47. Guadagni, F., Roselli, M. and Hoffman, R.M. Maintenance of expression of tumor antigens in three-dimensional *in vitro* human tumor gel-supported histoculture. *Anticancer Res.* 11, 543-546, 1991.
48. Hoffman, R.M. Three-dimensional gel-supported native-state histoculture for evaluation of tumor-specific pharmacological activity: Principles, practices and possibilities. *J. Cell. Pharmacol.* 2, 189-201, 1991.
49. Li, L. and Hoffman, R.M. Hair growth and hair follicle-cell-proliferation in histocultured mouse skin. *Annals of the New York Academy of Sciences, The Molecular and Structural Biology of Hair.* 642, 506-509, 1991.

50. Fu, X., Besterman, J.M., Monosov, A. and Hoffman, R.M. Models of human metastatic colon cancer in nude mice orthotopically constructed by using histologically-intact patient specimens. *Proc. Natl. Acad. Sci., USA* **88**, 9345-9349, 1991.
51. Li, L., Margolis, L.B. and Hoffman, R.M. Native-state sponge-gel histoculture of intact 3-dimensional tissue for *in vitro* toxicity assays. *Alternative Methods in Toxicology*, 8th International CAAT Symposium, (ed.) Alan M. Goldberg, The Johns Hopkins University. Vol. **8**, 311-316, 1991.
52. Fu, X., Theodorescu, D., Kerbel, R.S. and Hoffman, R.M. Extensive multi-organ metastasis following orthotopic onplantation of histologically-intact human bladder carcinoma tissue in nude mice. *Int J. Cancer* **49**, 938-939, 1991.
53. Baibakov, B., Frank, G.A., Sergeeva, N., Youngkin, T., Connors, K.M., Hoffman, R.M. and Margolis, L.B. *In vivo* growth patterns of human lung tumors in three-dimensional histoculture. *In Vitro Cell Dev. Biol.* **27A**, 897-899, 1991.
54. Hoffman, R.M. Altered regulation of transmethylation and loss of organotypic behavior in cancer. *Korean J. Biochem.* **23**, 83-89, 1991.
55. Li, L. and Hoffman, R.M. Eye tissues grown in three-dimensional histoculture for toxicological studies. *J. Cell. Pharmacol.* **2**, 311-316, 1991.
56. Furukawa, T., Kubota, T., Watanabe, M., Takahara, T., Yamaguchi, H., Takeuchi, T., Kase, S., Kodaira, S., Ishibiki, K., Kitajima, M. and Hoffman, R.M. High *in vitro-in vivo* correlation of drug response using sponge-gel-supported three-dimensional histoculture and the MTT end point. *Int. J. Cancer* **51**, 489-498, 1992.
57. Fu, X., Guadagni, F. and Hoffman, R.M. A metastatic nude-mouse model of human pancreatic cancer constructed orthotopically from histologically-intact patient specimens. *Proc. Natl. Acad. Sci., USA* **89**, 5645-5649, 1992.
58. Guadagni, F., Li, L. and Hoffman, R.M. Targeting antibodies to live tumor tissue in 3-D histoculture. *In Vitro Cell. & Dev. Biol.* **28A**, 297-299, 1992.
59. Fu, X. and Hoffman, R.M. Human RT-4 bladder carcinoma is highly metastatic in nude mice and comparable to ras^{H} -transformed RT-4 when orthotopically onplanted as histologically-intact tissue. *Int. J. Cancer* **51**, 989-991, 1992.
60. Wang, X., Fu, X. and Hoffman, R.M. A new patient-like metastatic model of human lung cancer constructed orthotopically with intact tissue via thoracotomy in immunodeficient mice. *Int. J. Cancer* **51**, 992-995, 1992.
61. Colangelo, D., Guo, H-Y, Silvestro, L. and Hoffman, R.M. Non-colorimetric measurement of cell activity in three-dimensional histoculture using the tetrazolium dye MTT: The pixel image analysis of formazan crystals (PIAFC). *Analytical Biochem.* **205**, 8-13, 1992.

62. Guo, H-Y., Colangelo, D., Li, L., Connors, K.M., Kubota, T. and Hoffman, R.M. *In vitro* histoculture of human tumors with fluorescent dye end-points measured by confocal microscopy: High correlation of *in vitro* and *in vivo* chemosensitivity. *Anticancer Res.* 12, 1055-1062, 1992.
63. Hoffman, R.M. Patient-like models of cancer in mice: A review and critique of their development. *Current Perspectives on Molec. & Cell. Oncol.* 1, Part B, 311-329, 1992.
64. Li, L., Paus, R., Margolis, L.B. and Hoffman, R.M. Hair growth *in vitro* from histocultured skin. *In Vitro Cell Dev. Biol.* 28A, 479-481, 1992.
65. Hoffman, R.M. Histoculture and the immunodeficient mouse come to the cancer clinic: Rational approaches to individualizing cancer therapy and new drug evaluation. *Int. J. Onc.* 1, 467-474, 1992.
66. Li, L., Margolis, L.B., Paus, R. and Hoffman, R.M. Hair shaft elongation, follicle growth, and spontaneous regression in long-term, gelatin sponge-gel-supported histoculture of human scalp skin. *Proc. Natl. Acad. Sci., USA* 89, 8764-8768, 1992.
67. Wang, X., Fu, X., Kubota, T., and Hoffman, R.M. A new patient-like metastatic model of human small-cell lung cancer constructed orthotopically with intact tissue via thoracotomy in immunodeficient mice. *Anticancer Res.* 12, 1403-1406, 1992.
68. Fu, X., Herrera, H., Kubota, T. and Hoffman, R.M. Extensive liver metastasis from human colon cancer in nude and SCID mice after orthotopic onplantation of histologically-intact humancolon carcinoma tissue. *Anticancer Res.* 12, 1395-1398, 1992.
69. Furukawa, T., Kubota, T., Watanabe, M., Kase, S., Takahara, T., Yamaguchi, H., Takeuchi, T., Kodaira, S., Ishibiki, K., Kitajima, M. and Hoffman, R.M. Chemosensitivity testing of clinical gastrointestinal cancers using histoculture and the MTT end point. *Anticancer Res.* 12, 1377-1382, 1992.
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